REMARKS

The Office Action mailed August 28, 2001, has been received and reviewed. Claims 25-34 are currently pending in the application. Claims 25-29 stand rejected. Claims 30-34 have been withdrawn from consideration. All amendments are made without prejudice or disclaimer.

Reconsideration of the referenced application is respectfully requested.

I. 35 U.S.C. § 102(e)

A. Squirrell

Claims 25, 26, 28, and 29 stand rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent 5,750,337 to Squirrell (hereinafter "Squirrel").

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Brothers v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). In the present case, the cited art fails to disclose the subject matter contained in the amended claims of the present invention.

Squirrell teaches, among other things, a method for detecting nucleic acid sequences that employs a cylindrical waveguide. As depicted in FIG. 1 of Squirrell, light from an external source is coupled into the waveguide from an end thereof. The light is reflected within the cylindrical waveguide in such a way as to generate an evanescent field adjacent to the surfaces thereof. Capture molecules that have been immobilized to the surface of the cylindrical waveguide then bind both analyte and fluorescently labeled tracer molecules within one or more sample and/or test solutions. The evanescent field excites the fluorescent labels of the bound tracer molecules, causing them to fluoresce. Some of the fluorescent light is then coupled back into the cylindrical waveguide, where it is internally reflected. FIG. 1 of Squirrell shows that this internally coupled fluorescence may then be detected as it exits, or outcouples, an end of the cylindrical waveguide.

Independent claim 25, as amended and presented herein, recites a fluorescence assay that includes, among other things, providing a waveguide with a "plurality of capture oligonucleotides *site-specifically immobilized* thereon . . .", "providing a detection element operably disposed to

directly radiated fluorescence emitted from molecules located adjacent to a surface of the waveguide . . .", and "selectively and *directly collecting radiated fluorescent light* emitted from the tracer molecules." (Emphasis supplied).

Squirrell lacks any express or inherent description of a fluorescent assay that includes providing a waveguide with capture oligonucleotides *site-specifically immobilized* thereto. Although Squirrell discloses, at col. 7, lines 44-55, that the surfaces of a waveguide may be silanized and treated with gluteraldehyde to facilitate covalent immobilization of oligonucleotides thereto, Squirrell does not describe that the capture oligonucleotides are covalently immobilized to specific sites, such as individual immobilizing molecules, on the waveguide surface.

Moreover, Squirrell does not expressly or inherently describe providing detection element that is operably disposed to *directly collect radiated fluorescence*. Instead, Squirrell quite clearly discloses that the assay method described therein includes providing a detection element oriented to sense fluorescence which has been coupled back into the waveguide, then outcoupled from the waveguide. Thus, Squirrell teaches a fluorescence assay in which the fluorescence emitted from molecules located adjacent to a surface of the waveguide is *indirect collected* fluorescence which has been *internally reflected* within the waveguide.

For the same reason, Squirrell neither expressly nor inherently describes "selectively and directly collecting radiated fluorescent light emitted from the tracer molecules."

Accordingly, it is respectfully submitted that Squirrell does not anticipate each and every element of amended independent claim 25, as is required to maintain a rejection under 35 U.S.C. § 102(e). Therefore, under 35 U.S.C. § 102(e), amended independent claim 25 is allowable over Squirrell.

Claims 26, 28, and 29 are each allowable, among other reasons, as depending either directly or indirectly from claim 25, which is allowable.

Claim 26 is further allowable since Squirrell includes no express or inherent description of a fluorescent assay in which "a single moiety . . . on each capture molecule" is modified "to produce activated capture oligonucleotides having a modified moiety constructed to be coupled to the first coating . . ." or in which a coated surface of the waveguide is treated "with the activated capture

oligonucleotides under conditions to cause the modified moiety to couple to the first coating and thereby immobilize the activated capture oligonucleotides to the waveguide surface."

Claim 28 is additionally allowable since Squirrell does not expressly or inherently describe that "an oligonucleotide primer acting as a capture oligonucleotide complementary to [an] analyte is immobilized to [a] waveguide by amine-reactive, thiol-reactive, or (strep) avidin-biotin coupling chemistry."

B. Bouma

Claims 25, 26, 28, and 29 also stand rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent 5,585,242 to Bouma et al. (hereinafter "Bouma").

Again, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Brothers v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). In the present case, the cited art fails to disclose the subject matter contained in the amended claims of the present invention.

Bouma also describes a fluorescent assay method in which a cylindrical waveguide is used. The method described in Bouma includes effecting binding between a capture oligonucleotide and an analyte in a polymerase chain reaction (PCR) chamber. As shown in FIG. 2 of Bouma, light that is coupled into an end of the cylindrical waveguide is reflected internally therein and results in an evanescent field adjacent to external surfaces of the cylindrical waveguide. Fluorescently labeled tracer molecules that bind to immobilized capture olignonucleotide molecules are excited by the evanescent field and, thus, fluoresce. Some of the fluorescent light is coupled back into the cylindrical waveguide. When this fluorescent light is outcoupled through one or both ends of the cylindrical waveguide, it may be detected by a properly positioned detector.

To reiterate, amended independent claim 25 recites a fluorescence assay that includes, among other things, "providing a detection element operably disposed to *directly collect radiated fluorescence* emitted from molecules located adjacent to a surface of the waveguide . . .", and

"selectively and *directly collecting radiated fluorescent light* emitted from the tracer molecules." (Emphasis supplied).

Bouma does not expressly or inherently describe providing detection element that is operably disposed to *directly collect radiated fluorescence emitted* from molecules that are located adjacent to a surface of a waveguide. Rather, the assay method of Bouma quite clearly includes providing a detection element oriented to collect fluorescence which has been coupled back into the waveguide, then outcoupled from an end of the waveguide. Thus, such fluorescence is not *directly collected radiated fluorescence*, it is *indirectly collected* fluorescence which has been *internally reflected.*

For the same reason, Bouma neither expressly nor inherently describes "selectively and *directly collecting* fluorescent light emitted from the tracer molecules . . ." thereof.

It is, therefore, respectfully submitted that Bouma does not anticipate each and every element of amended independent claim 25, as is required to maintain a rejection under 35 U.S.C. § 102(e). Therefore, under 35 U.S.C. § 102(e), amended independent claim 25 is allowable over Bouma.

Claims 26, 28, and 29 are each allowable, among other reasons, as depending either directly or indirectly from claim 25, which is allowable.

For these reasons, it is respectfully requested that the 35 U.S.C. § 102(e) rejections of claims 25, 26, 28, and 29 be withdrawn.

II. 35 U.S.C. § 103(a)

A. Squirrell in View of Wybourne

Claim 27 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Squirrell in view of U.S. Patent 5,465,151 to Wybourne et al. (hereinafter "Wybourne").

It is respectfully submitted that, to establish a *prima facie* case of obviousness under 35 U.S.C. § 103(a), three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the cited prior art reference must teach or

suggest all of the claim limitations. Furthermore, the suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on Applicants' disclosure.

The teachings of Squirrell are summarized above.

Wybourne teaches, among other things, an assay that employs a technique known as interferometry to detect the presence of analytes in a sample. A waveguide that is useful in interferometry, as illustrated in FIG. 1 of Wybourne, includes an incoming section, a first junction where the waveguide splits into two adjacent sections, a second junction where the two sections converge, and an outgoing section, from which light is detected. One of the two adjacent sections of the waveguide is used as a reference, while the other of the two adjacent sections is used to detect the amount of analyte, if any, present in a sample. The reference section does not have capture molecules immobilized relative thereto. The detection section does have capture molecules immobilized thereto. As light passes through the waveguide, the characteristics of the light that passes through the detection section thereof are altered, making the light that has passed through the detection section different than that which has traveled through the reference section. These differences are detected as light is coupled out of the waveguide through the outgoing section thereof and are indicative of the amount of analyte present in a sample solution.

Claim 27 is allowable, among other reasons, as depending from claim 25, which is allowable.

Additionally, it is respectfully submitted that one of ordinary skill in the art would not have been motivated to combine the teachings of Squirrell and Wybourne in the manner that has been asserted. Specifically, it is respectfully submitted that one of ordinary skill in the art would not have been motivated to modify a fluorescence assay with teachings that relate to an interferometry assay.

It is also respectfully submitted that Wybourne does not remedy the deficiencies of Squirrell with respect to providing a detection element that is operably disposed to *directly collect radiated fluorescence* emitted from molecules located adjacent to a surface of a waveguide. Like Squirrell, light that is coupled out of the interferometry waveguide of Wybourne is *indirectly collected* fluorescence which has been *internally reflected* within the interferometry waveguide, then outcoupled from an end thereof. Thus, Wybourne does not teach or suggest providing a detection element to *directly collect radiated fluorescent light*, as recited in amended independent claim 25,

from which claim 27 depends. Nor does Wybourne teach or suggest "selectively and *directly collecting radiated fluorescent light* emitted from the tracer molecules . . ." thereof.

Moreover, neither Squirrell nor Wybourne teaches or suggests a first waveguide coating "selected from the group consisting of: avidin, biotin, a hydrogel formed of polymethacryloyl polymers, and a modified polyethylene glycol", as recited in claim 27.

It is, therefore, respectfully submitted that the Office has not established a *prima facie* case as to the obviousness of claim 27 and that, under 35 U.S.C. § 103(a), claim 27 is allowable over the combination of Squirrell and Wybourne.

B. Bouma in View of Wybourne

Claim 27 also stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Bouma in view of Wybourne.

The teachings of both Bouma and Wybourne are summarized above.

Among other reasons, claim 27 is allowable as depending from claim 25, which is allowable.

Claim 27 is further allowable since one of ordinary skill in the art would not have been motivated to combine the fluorescence assay of Bouma with the interferometry assay of Wybourne.

Additionally, it is respectfully submitted that Wybourne does not remedy the deficiencies of Bouma with respect to teaching detection element that is operably disposed to *directly collect radiated fluorescence* emitted from molecules located adjacent to a surface of a waveguide. Rather, Wybourne is like Bouma with regard to the fact that the methods taught in both of these references include the *indirect collection* of fluorescent light: the light that is detected in both Bouma and Wybourne has been *internally reflected* within and subsequently coupled out of their respective waveguides. Thus, neither Bouma nor Wybourne teaches or suggests providing a detection element in such a way as to *directly collect radiated fluorescent light*, as recited in amended independent claim 25, from which claim 27 depends. Nor does Wybourne teach or suggest "selectively and *directly collecting radiated fluorescent light* emitted from the tracer molecules . . ." thereof.

For these reasons, it is respectfully submitted that the Office has not established a *prima facie* case as to the obviousness of claim 27 and that, under 35 U.S.C. § 103(a), claim 27 is therefore allowable over the combination of Bouma and Wybourne.

In view of the foregoing, it is respectfully requested that the Office withdraw the 35 U.S.C. § 103(a) rejections of claim 27.

CONCLUSION

It is respectfully submitted that each of claims 25-29 is allowable. An early notice of the allowability of each of these claims is respectfully solicited, as is an indication that the referenced application has been passed for issuance. If any issues preventing the allowance of any of claims 25-29 remain which might be resolved by way of a telephone conference, the Office is kindly invited to contact the undersigned attorney.

Respectfully submitted,

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Encl: Version with markings to show changes made

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

A marked up version of each of the presently amended claims, highlighting the changes thereto, follows:

25. (Twice amended) A fluorescence assay, comprising the steps of:

providing a waveguide which is optically conductive and which has at least one surface having a plurality of capture oligonucleotides site-specifically immobilized thereon, wherein [said] the capture oligonucleotides have a binding site which selectively binds a selected analyte;

providing a light source operable to emit a light beam in a desired wavelength range and positioned to send light into the waveguide;

providing a detection [means] element operably disposed [for detecting] to directly collect radiated fluorescence emitted from molecules located adjacent to a surface of the waveguide;

providing a sample comprising a buffer and a plurality of molecules of a selected analyte;

providing a plurality of tracer molecules which are operable to emit fluorescence in response to stimulation by [light from the light source] an evanescent field adjacent to a surface of the waveguide;

combining the sample with the tracer molecules to produce a test solution;

placing the test solution in contact with the waveguide surface while operating [said] the light source to direct light into the waveguide to generate the evanescent field; and

selectively and directly collecting radiated [detecting] fluorescent light emitted from the tracer molecules.